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RECORD OF ORAL HEARING

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte RONALD J. PETTIS, JAMES A. DOWN,
and NOEL G. HARVEY

Appeal 2010-006501
Application 09/606,909
Technology Center 3700
Oral Hearing Held: October 16, 2012

Before LINDA E. HORNER, STEVEN D.A. McCARTHY,
and GAY ANN SPAHN, *Administrative Patent Judges*.

APPEARANCES:

ON BEHALF OF THE APPELLANT:

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The above-entitled matter came on for hearing on Tuesday, October 16, 2012, commencing at 1:05 p.m., at the United States Patent and

Trademark Office, 600 Dulany Street, Alexandria, Virginia, before Diane Humke.

P R O C E E D I N G S

THE USHER: Calendar No. 30, Appeal No. 2010-6501, Ms. Coruzzi.

JUDGE HORNER: Thank you.

JUDGE HORNER: Okay. We've had an opportunity to review the case and you've got 20 minutes, and you can proceed when you're ready.

MS. CORUZZI: Okay. Thank you very much. It's a privilege to be in your room today. I'm here just to introduce my colleagues. Markus Bergauer is an associate at Jones Day who has worked on this case with me, and Robert West is a senior patent agent at Becton Dickinson, the assignee of the patent application involved. I'll try to stay in my 20 minutes allotted but beg your indulgence if we run over time.

This case is about the administration of insulin to a human subject into the intradermal compartment, resulting in a systemic distribution in the bloodstream superior to standard subcutaneous delivery. The sole issue on appeal is obviousness. There were obviousness-type double patenting rejections that are moot because those applications are now abandoned.

The examiner erroneously reached the conclusion of obviousness based on three reversible errors: hindsight reconstruction, the examiner unreasonably interpreted the claim term bioavailability and failed to consider unexpected results in the record. If you should agree with me on any one of those, you must reverse.

The claims at issue encompass administering insulin to a subject through a hollow needle that penetrates the dermis of the subject's skin so

that the depth and exposed height of the outlet of the needle, which I'm going to say is the orifice so that I don't have to keep saying depth and exposed height of the outlet, is contained within a narrow target within the dermis and then applying a pressure that's effective to control the rate of delivery so that a specific what we call PK distribution of the drug is achieved.

Two requirements of the pharmacokinetic, PK, profile are required by the claim: a higher maximum plasma concentration, which is also called C(max), and a higher bioavailability, which is defined as the area under the curve, which I may refer to as AUC.

JUDGE HORNER: Okay. My understanding is one of the points of contention here we need to decide is whether bioavailability is equivalent to AUC or whether there are other means by which to determine bioavailability.

MS. CORUZZI: Right. I mean, why don't we go to that point right now. So, in this record, we've put in treatises, the Merck manual, that define AUC as the most reliable measure of bioavailability. The Kasting declaration, this is in the evidence appendix at E-194, he indicates that Claim 29, which recites the requirement of increased bioavailability, requires an increased AUC, so he's equating AUC with bioavailability. And he, by the way, is a Ph.D. from MIT. He's in the field at I think Procter & Gamble, a reviewer of peer-reviewed journals. So he came to the conclusion that Claim 29 requires a higher AUC.

JUDGE HORNER: And is the only place we find that is to sort of infer it from the statement in paragraph 19, or does he come out somewhere else in this declaration and state, you know --

MS. CORUZZI: No, it's in paragraph 19 when he states that the claim requires an increased AUC. I'll find it for you in one second. Paragraph 19 on page 9, for example, Autret's pharmacokinetic profile does not exhibit both an increased C(max) and an increased AUC, as required by the claims of the Pettis application. So he's come to that conclusion.

There's another issue. In our reply brief at page 15, we address the issue of the claims require both a C(max) increase and an increase in bioavailability. The examiner contends that either one of those is a measure of bioavailability. If that were the case, then our two limitations are redundant and it's improper to read a claim to make one limitation superfluous. And there are a number of recent Board of Appeals decisions that have come down since our briefing. If I can read them into the record?

JUDGE HORNER: Yes.

MS. CORUZZI: Ex parte Mancie -- I have the Westlaw cites, I can read that in -- 2012 Westlaw 407888; Ex parte Sexton, 2012 WL 334461; and Ex parte Shukla, 2012 WL 1089015. And these all cite to a case called Stumbo v. Ameristep, and that's a Federal Circuit decision, 508 F.3d 1358. So since the claim requires two limitations to be elevated, if you took the examiner's position, one of our limitations would be superfluous. That's error, and we think it should be reversed.

JUDGE HORNER: What about the statement in the Merck excerpt that says the most widely used general index of absorption rate is peak time, so not C(max) but T(max) being an indicator of bioavailability?

MS. CORUZZI: But I believe the Merck manual goes on to say that either T(max) -- here we go. However, peak time is often not a good statistical measure because it's a discrete value that depends on frequency of blood sampling, and in the case of relatively flat concentrations near the peak, on assay reproducibility.

And with respect to C(max), the Merck manual says -- this is, I'm sorry, E-122, page 2560 of the Merck manual, first column where it says assessment of bioavailability. Bioavailability determinations based on peak plasma concentration can be misleading because drug elimination begins as soon as the drug enters the bloodstream. So the C(max) is the peak of when absorption equals elimination, and the Merck manual says don't use that for determining bioavailability. It's a measure you take to ultimately come to a conclusion about bioavailability, but according to Merck, AUC is the most reliable measure of bioavailability.

And we also relied on the Federal Circuit decision in Abbott v. Sandoz, and this is in our brief at pages 17 to 18. And I'm not relying on it for res judicata but for the fact that in a case at a similar time period involving drug delivery, the Court, the District Court and the Federal Circuit agreed that AUC is the measure for bioavailability, and that was uncontested by the parties involved in the Abbott v. Sandoz case. So that's an external data point if you will of evidence of how the skilled artisan would interpret bioavailability and AUC. And again, that's in our brief at pages 17 to 18.

JUDGE MCCARTHY: But, counsel, I'm reading the passage from the Merck manual here and it looks to me that they are conceding that the most widely used general index of absorption rate is peak time, but then they're giving their own opinion that AUC is better. Is there anything to suggest in this passage that AUC is generally recognized as being a better measure?

MS. CORUZZI: Well, I think the Merck manual is not just an opinion, I think it's a treatise that the skilled workers look to, and I think the Abbott v. Sandoz case is evidence of how workers in the field at the time period, same time period as our filing date, viewed AUC as the measure of bioavailability, as did Autret. I'm going to try my French. Biodisponibilité was measured as AUC. Not C(max), not T(max), but AUC. And Autret is one of the main references that the examiner's relying on. Did that answer your question?

JUDGE MCCARTHY: Yes. Thank you.

MS. CORUZZI: Okay. Great. So using this nonconventional, incorrect interpretation of bioavailability, then the examiner makes the mistake of coming to the conclusion that Autret is the only reference that reports a PK, none of the other references even report a PK or have a PK, the vaccine art doesn't use PKs at all, vaccines are injected locally, cells eat up the antigen and then travel into the lymphatic system. You don't have a PK in the bloodstream, which is required by the claim. So Puri, D'Antonio and Srivastava, you know, are just incorrect. It's an incorrect use of those references. Autret is the only one, and in plain I would have said English, but it's French, he basically says that there's no difference in bioavailability

(biodisponibilité), between subcutaneous and intradermal injections. Mesotherapy was what it was called in the Autret reference.

So the examiner is taking the position that because Autret has an increased C(max), and in his definition C(max) qualifies as equal to bioavailability, that's his sole basis for saying Autret.

JUDGE HORNER: But doesn't Autret also have a lower T(max), so it's got a faster absorption?

MS. CORUZZI: Well, T(max) is not -- hang on. Possibly. It's hard for me to tell from the graph whether the ID occurred faster.

JUDGE HORNER: I think it was in the description.

MS. CORUZZI: He doesn't mention T(max) at all as far as I can tell from the translation and the little bit of French that I can read, but he does indicate that there's an increased C(max) but no difference in bioavailability. And if you look at Table 1B3, you see the columns are ID, which is intradermal, sub-Q, which is SC, BD, which is the French biodisponibilité, which means bioavailability, and he finds no difference between sub-Q injections and ID.

And again in the conclusion, in the discussion and conclusion on page E4, Autret concludes in the discussion that these facts speak against a more rapid or greater resorption put forward to justify mesotherapy, in other words, ID, and that's in Column 1. And then the conclusion, it says in black and white in French that there's a difference -- and this is calcitonin, not insulin, but because we're talking about obviousness, we're considering it -- there's a difference in the C(max), but the biodisponibilité, bioavailability, is not different after ID injection as opposed to sub-Q injection.

JUDGE HORNER: It seems like Autret is saying, and I'm looking at page 4 of the translation under the section entitled Results, that T(max) is at 23.6, plus or minus 10 minutes with the subcutaneous route and 16.2, plus or minus 7.5 minutes, with the ID route, and then later in more detail on page 6 they explain that for three of the subjects in the study, T(max) was earlier with ID, whereas for three others it appeared at the same time, whatever the route of administration. So it seems like at least in some of the subjects T(max) was earlier, and then they say the average C(max) is significantly higher with the ID route than with the subcutaneous route. So it seems like if we were to take bioavailability, which we measure by T(max) or area under the curve under the broadest reasonable interpretation, then Autret would meet the claim because T(max) is earlier, which would show it's got greater bioavailability than with the subcutaneous route.

MS. CORUZZI: Well, it's still an unreasonable interpretation of this claim. When we first set out, we had a broader claim and we had dependent claims for C(max), T(max) and AUC. The examiner restricted us out and made us pick one, and we picked the one with the two parameters, C(max) and bioavailability, which we've always interpreted as AUC. So even the examiner given that restriction could not be looking at T(max), nor did he in interpreting Autret. The examiner's position is that bioavailability can be measured by
C(max) or the AUC, and that's the reason he's picking on Autret.

JUDGE HORNER: But he says in page 5 of the answer, Autret discloses intradermal injection of a hormone resulting in a pharmacokinetic profile similar to subcutaneous delivery but with a higher plasma level and

bioavailability, as assessed by C(max) and T(max), and he points to Figure 1. So I understand that to mean he's looking at T(max) as the measure of bioavailability.

MS. CORUZZI: I'm sorry, where are you in the --

JUDGE HORNER: I'm on page 5 of the answer.

MS. CORUZZI: Page 5 of the answer.

JUDGE HORNER: The second full paragraph.

MS. CORUZZI: But Autret doesn't use T(max) as a parameter for reaching the conclusion that bioavailability is the same or different in his experiment. And if you go to Table 1 of Autret, again, he's equating AUC -- I mean, the table says AUC, ID, sub-Q and then biodisponibilité, which is bioavailability. So Autret is not using T(max) at all in his discussion of bioavailability and in his statement concerning no difference in bioavailability between ID and sub-Q. And again, the Merck manual discounts T(max) as a way to measure bioavailability, so that would be consistent with the treatise that the skilled artisan would look at.

I mean, the examiner is trying, I mean, he's trying to use C(max) and T(max). He's wrong, and that's evidenced by Merck, Autret itself, which does not use either C(max) or T(max) when it discusses biodisponibilité or bioavailability. And again, the examiner's 103 analysis hinges on this incorrect interpretation of bioavailability. So you could drag in Autret and say don't mind what Autret says, just look at these two numbers that Autret himself did not use when Autret was describing bioavailability.

So, if you agree with me that the examiner has taken an unreasonable interpretation of the claim, then you should reverse on the basis that Autret

just doesn't fit the bill. None of the references have a PK, that's the only one with a PK, and its PK does not fit the requirement of the claim. And that's also underscored by Dr. Kasting, who interpreted the claim as requiring an increased AUC and came to the conclusion that Autret does not have what it takes to anticipate the claim or make it obvious.

JUDGE HORNER: Okay. Well, we've run up against your 20 minutes, so if you want to wrap up.

MS. CORUZZI: Okay. I guess the other thing, if we can, the other problem that the examiner has engaged in is hindsight reconstruction. And it's all briefed, but I think one of the most egregious things is he's just taken measurements from our application and grafted them into the prior art without any explanation of how you get there. And I've tried to calculate and figure out how did he get these numbers. He got the numbers from our specification.

JUDGE HORNER: And you're talking about the length of the needle now?

MS. CORUZZI: Right.

JUDGE HORNER: Okay.

MS. CORUZZI: The needle outlet. And in essence, I think here, if you look at 103, which is the only issue here from the KSR point of view, 103 bars patentability unless the improvement is more than the predictable use of prior art elements according to their established function. So, in our case, there's no known relationship between the orifice and the requirement of keeping the orifice in that narrow targeted area and the resulting PK when the appropriate pressures are applied. So, in the absence of that known

relationship, it can't be said that this is routine experimentation of known variables because it was an unknown variable. That's the invention. And a case I'd like to cite that I think supports us on this is the recent Federal Circuit decision In re: Cyclobenzaprine, 676 F.3d 1063, and that just came down I think this month. Thank you. Sorry. April 2012. And another recent Board decision, Ex parte McLaughlin, and this is Appeal No. 2009-001294.

So here, hindsight reconstruction, incorrect claim construction, to cobble together a facsimile of the invention that doesn't really exist in the prior art.

JUDGE HORNER: Okay.

MS. CORUZZI: Okay.

JUDGE HORNER: Thank you.

MS. CORUZZI: Thank you.

(Whereupon, at 1:30 p.m., the proceedings were concluded.)